Non-technical Abstract

HIV infection leads to destruction of a person's immune system, primarily through loss of T-lymphocytes. T-lymphocytes and other important cells of the immune system are constantly being generated from very specialized progenitor cells found in the bone marrow. In HIV infected persons, these progenitor cells cannot produce new T-lymphocytes as fast as they are killed by the HIV virus. This study will ask if genetically engineered progenitor cells can give rise to T-lymphocytes that are less likely to be killed by infection with HIV. To do this, progenitor cells will be made to leave the bone marrow and enter the blood stream by the use of a stimulatory drug. Progenitor cells will then be obtained from a blood sample obtained by a procedure similar to a blood donation. These progenitor cells will be cultured for 3 to 4 days on other cells previously obtained from the person's bone marrow. During this time the progenitor cells will be treated with cytokines that insure that the progenitor cells remain healthily. The progenitor cells will then be genetically engineered by treatment with a modified retrovirus that carries a gene encoding for two ribozymes. The retrovirus does not contain any virus genes, is not capable of replicating or spreading to other cells and is not related to the HIV virus. The ribozymes are a special type of RNA capable of finding and destroying HIV RNA. Cells that contain these ribozymes may be protected from HIV infection. Additional progenitor cells will be treated with a similar retrovirus, but lacking the ribozyme gene. The engineered cells will then be given back to the patient in a manner similar to a blood infusion. We will then monitor the patient for cells in the bloodstream derived from these engineered progenitor cells to determine if progenitor cells that carry the ribozyme will give rise to T-lymphocytes that live longer than those that are not genetically engineered or those that were treated with the retrovirus that lacks the ribozyme.